REMARKS

Claims 1, 3, 8 and 10 have been amended. Claims 2, 11 and 12 have been canceled. New claims 30 and 31 have been added. Claims 4-7, 13-20 and 22-29 have been withdrawn from consideration as being directed to non-elected inventions. Thus, claims 1, 3, 8-10, 21, 30 and 31 are now presented for examination. Support for the amendment to claim 1 may be found in the specification at, for example, page 8, lines 16-18; and page 9, lines 15-34; pages 22-25, and in original claim 3. Support for the amendment to claim 8 may be found in the specification at, for example, page 12, line 30 to page 13, line 5; and page 22, line 30 to page 25, line 18. Support for new claims 30 and 31 may be found in claim 1. Thus, no new matter has been introduced by these amendments.

Claim objections

Claims 1 and 11 were objected to as reciting non-elected subject matter. Claim 11 has been canceled, and claim 1 as amended recites only elected subject matter, thus overcoming these objections.

Rejection under 35 U.S.C. §101

The Examiner rejected claims 1 and 11, alleging that they recited non-statutory subject matter since the claims do not state that the protein has been isolated. Claim 11 has been canceled, and claim 1 as amended recites that the protein is isolated.

In view of the comments presented above, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §101.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1-3, 8-12 and 21 as allegedly being indefinite based on identification of a protein solely by name (e.g., apolipoprotein L-1), rather than other more definite characteristics (e.g., structural properties, molecular weight and/or source); Claims 11 and 12 have been canceled, thus rendering the rejections moot as they apply to these claims. Claim 1, and the claims that depend directly or indirectly thereon, identify the protein by sequence (SEQ ID NO: 1) rather than by name.

Claim 1 was rejected as being indefinite based on recitation of "adequate", since it was allegedly unclear what was encompassed by this terminology. Although Applicants submit that one of ordinary skill in the pharmaceutical art would clearly realize the metes and bounds of such compositions, the claim as amended recites "a pharmaceutically acceptable carrier or diluent", rather than "an adequate pharmaceutical carrier or diluent."

The Examiner rejected claim 2, stating that it was unclear what was meant by the protein "corresponding to SEQ ID NO: 1." Claim 2 has been canceled, thus rendering this rejection moot.

Claims 1 and 3 were rejected based on recitation of the phrase "pharmaceutically active fragment." Claim 1 as amended no longer recites this phrase. Claim 3 as amended recites "trypanolytically active fragment", rather than pharmaceutically active fragment.

Claim 12 was rejected as indefinite based on recitation of the phrase "an homologue polypeptide." Claim 12 has been canceled, thus rendering this rejection moot.

In view the comments presented above, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-3, 8-12 and 21 under 35 U.S.C. § 112, first paragraph, stating that "while being enabling for "an isolated polypeptide comprising SEQ ID NO: 1 (and the specific fragments recited in claim 3)" does not reasonably provide enablement for pharmaceutical compositions comprising *any* apolipoprotein L-1..." The Examiner also alleges that the specification is not enabled for treatment of any disease by any species of Trypanosoma using these pharmaceutical compositions.

Applicants respectfully disagree with these allegations. Claim 1 as amended recites a pharmaceutical composition comprising an isolated polypeptide having greater than 95% sequence identity to the polypeptide of SEQ ID NO: 1, or to trypanolytically active fragments thereof. One of ordinary skill in the art will appreciate that any desired fragment of SEQ ID NO: 1 can be produced using methods well known to one of skill in the art, and evaluated for trypanolytic activity as disclosed in the specification at pages 19-25 without undue experimentation. In addition, proteins having at least 95% identity to SEQ ID NO: 1 can be made using mutagenesis techniques well known in the art, and these polypeptides can also be

evaluated for activity as described in the specification. Although generation of such fragments, and testing these for trypanolytic activity would be tedious, these are standard protocols well known in the art of and cannot be considered to involve undue experimentation. According to M.P.E.P. § 2164.01, the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm"n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).

In addition, Applicants do not agree that the specification is not enabled for treatment of any diseases caused by any species of Trypanosoma. The specification clearly enables a method of ameliorating and/or preventing a Trypanosoma infection in a mammal by administering a pharmaceutical composition comprising the isolated polypeptide of claim 1, or a trypanolytically active fragment thereof. These methods are clearly enabled and described in the present specification at page 22, line 30 to page 25, line 18, for two species of Trypanosoma, namely *Trypnosoma brucei rhodesiense* and *Trypanosoma brucei brucei*. One of ordinary skill in the art will appreciate that the trypanolytic activity of these peptides will necessarily prevent and/or cure trypanosome-mediated diseases since lysis of the causative agents will result in amelioration and/or the inability of these organisms to infect a mammal.

Claims 1-3, 8-12 and 21 were rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. The Examiner contends that only SEQ ID NO: 1 is described in the present specification, which is clearly incorrect. The specification as filed discloses various polypeptide fragments of SEQ ID NO: 1 (see page 3, lines 1-6; page 10, lines 4-10, page 18, lines 15-21).

Such language has been widely accepted by the PTO as noted in the 2008 Written Description guidelines which state, in Example 11A, that a claim to an isolated nucleic acid sequence that encodes a polypeptide with at least 85% sequence identity to SEQ ID NO: 2 is described by a specification that discloses a polynucleotide sequence of SEQ ID NO: 2. The guidelines state that "the disclosure of SEQ ID NO: 2 combined with the pre-existing knowledge in the art regarding the genetic code and its redundancies would have put one in possession of the

genus of nucleic acids that encode SEQ ID NO: 2. With the aid of a computer, one of skill in the art could have identified all of the nucleic acids that encode a polypeptide with at least 85 % sequence identity with SEQ ID NO: 2. Thus, one of ordinary skill in the art would conclude that the applicant was in possession of the claimed genus at the time the application was filed."

In view of the comments presented above, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph.

Rejections under 35 U.S.C. § 102(b)

Claims 1-3, 11 and 12 were rejected under 35 U.S.C. §102(b) as being anticipated by Duchateau et al. (*J. Lipid Res.* 42:620-630, 2001). The Examiner alleges that a recitation of intended use must result in a structural difference between the claimed invention and the prior art in order to patentable, and that if the prior art structure is capable of performing the intended use, then it meets the claim. In the present case, the Examiner states that a "pharmaceutical carrier" or "diluent" reads on water, and would therefore be inherent in the preparation/isolation of the proteins.

Ducati et al. disclose characterization of the genes encoding the Apo-L family of proteins, including pail-I. This reference describes axon structure, splice variants, transcriptional start sites, and expression in several tissues using degenerate primers. However, this reference does not disclose isolation or purification of any pail-I protein or polypeptide. Because this reference does not disclose that the protein was ever isolated, it also does not disclose placing the protein into any type of carrier, buffer or solution. In order for a claim to be anticipated by a reference, thee reference must disclose every element of the claim. In the present case, Ducati et al. do not disclose the isolated protein or any fragment thereof, or any pharmaceutically acceptable carrier containing the isolated protein or any fragment thereof . In addition, this reference provides absolutely no teaching or suggestion that such a protein would have any pharmaceutical activity. Thus, its placement into a pharmaceutically acceptable carrier would also not be obvious in view of this reference.

Claims 1-3, 11 and 12 were rejected as allegedly anticipated by Tyler et al. (*Mol. Biochem. Parasite.* 69:9-17, 1995). The Examiner states that although Tytler et al. do not specifically recite that their human apolipoprotein comprises SEQ ID NO: 1, that absent evidence to the contrary, it inherently would be given that it is from the same source, possesses the

identical function and name. Enclosed herewith as Exhibits A and B are the International Preliminary Examination Report (IPER) and International Search Report (ISR), respectively, in corresponding PCT Application No. PCT/BE2003/000131 (Publication No. WO 2004/012757). As noted in the IPER, the protein described by Tytler et al. is not the same as the protein in present claim 1. In item 6 of the IPER, the Examiner states that:

> The Applicant has however argued that the teaching of document D1 is in fact erroneous since the molecule identified in document D1 as apoL-I is not apoL-I but is a different molecule. The Applicant has pointed to the discrepancy between the apparent molecular weight of apoL-I as derivable from Figure 2c in D1 (greater than 80 kDa), and the molecular weight of apoL-I indicated in document D3 (42kDa) as support for this view. Thus, in the absence of any contrary evidence showing that the molecule described in document D1 was apo-LI, the International Examining Authority have accepted the arguments of the Applicant. Thus, it appears that the erroneous teaching of (the) document cannot for(m) the basis for a finding of lack of inventive step in respect of the subject matter of present Claims 1 to 10.

As noted in the ISR, document D1 corresponds to Tytler et al. (*Mol. Biochem. Parasitol.* 69:9-17, 1995), and document D3 corresponds to Duchateau et al. (*J. Lipid Res.* 42:620-630, 2001). Thus, because the claimed protein is not the same as the one disclosed by Tytler et al., the claims cannot be anticipated by this reference.

In view of the comments presented above, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(b).

CONCLUSION

Applicants submit that all claims are in condition for allowance. If any minor matters remain that could be resolved by teleconference, the Examiner is invited to contact the undersigned at the telephone number provided below. Please charge any additional fees, including any fees for extensions of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 7/18/08

By: 

Neil S. Bartfeld, Ph.D.
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EXHIBIT A

PATENT COOPERATION TREATY

PCT

REC'D 22 OCT 2004
WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P.ULB.91/WO		
International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/BE 03/00131	04.08.2003	02.08.2002

International Patent Classification (IPC) or both national classification and IPC
A61K38/17

Applicant
UNIVERSITE LIBRE DE BRUXELLES et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14.02.2004	21.10.2004
Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Pilling, S Telephone No. +49 89 2399-8461

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/BE 03/00131

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-29 as originally filed

Sequence listings part of the description, Pages

1-5 as originally filed

Claims, Numbers

1-16 as originally filed

Drawings, Sheets

1/6-6/6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

☐ restricted the claims.

☒ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. 1-10,14-16 .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10,14-16
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-10,14-16
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-10,14-16
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item IV
Lack of unity of invention

1. In agreement with the findings of the International Searching Authority (See the comment accompanying the INVITATION TO PAY ADDITIONAL FEES), it is considered that there is lack of unity of invention (Rule 13.1 PCT) in respect of the present claims. In this regard, there is no technical relationship involving one or more of the same or corresponding special technical features (Rule 13.2 PCT) between the subject-matter of the following groups of claims:

   a) Claims 1 to 10; pharmaceutical compositions/uses comprising apolipoprotein L-I (apoL-I), an active fragment thereof, a polynucleotide encoding apoL-I, a cell transformed with the latter polynucleotide or an apoL-I inhibitor

   b) Claims 11 to 13; diagnostic kits comprising apoL-I, a fragment thereof, a polynucleotide encoding apoL-I or an apoL-I inhibitor

   c) Claims 14 to 16; non-human genetically modified mammals which express a polynucleotide encoding apoL-I or a fragment thereof and are resistant to Trypanosomal diseases

   d) Claims 17 or 18; solid supports/methods for recovering apoL-I from a mammal using an immobilised apoL-I inhibitor

2. The following examination has been carried out in respect of inventions (a) and (c) as identified above for which International Search and Preliminary Examination fees have been paid.

Re Item V
Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

3. The documents cited in the International Search Report (ISR) are consecutively numbered D1 to D7 in the order of their listing. If not indicated otherwise, reference is made to the passages cited in said ISR.

invention (a)

4. None of the presently available prior documents discloses pharmaceutical compositions comprising apolipoprotein L-I (apoL-I), an active fragment thereof, a polynucleotide encoding apoL-I, a cell transformed with the latter polynucleotide or an apoL-I inhibitor. Thus, the subject matter of Claims 1 to 10 is new (Article 33(2) PCT).

5. The closest prior art in respect of Claims 1 to 10 appears to be document D1 since this document discloses that apoL-I is a trypanolytic factor (TLF) in human blood (see the abstract). Document D1 further indicates "*The potential of exploiting a natural non-immune killing factor, TLF as an alternative chemotherapy for African trypanosomiasis deserves further investigations*" (see the final paragraph of the Discussion). Thus, it appears *prima facie* that document D1 suggests the administration of a medicament based on apoL-I.

6. The Applicant has however argued that the teaching of document D1 is in fact erroneous since the molecule identified in document D1 as apoL-I is not apoL-I but is a different molecule. The Applicant has pointed to the discrepancy between the apparent molecular weight of apoL-I as derivable from Figure 2c in D1 (greater than 80 kDa) and the molecular weight of apoL-I indicated in document D3 (42kDa) as support for this view. Thus, in the absence of any contrary evidence showing that the molecule described in document D1 was apoL-I, the International Examining Authority have accepted the arguments of the Applicant. Thus, it appears that the erroneous teaching of document cannot for the basis for a finding of lack of inventive step in respect of the subject matter of present Claims 1 to 10.

7. None of the further pre-published documents disclose that apoL-I is a trypanolytic factor.

8. Thus, the subject matter of Claim 1 to 10 appears to be inventive (Article 33(3) PCT).

Invention (c)

9. None of the presently available prior art documents disclose a genetically modified mammal expressing an apoL-I polynucleotide/polypeptide. Thus, the subject matter of Claims 14 to 16 is new.

10. None of the presently available prior art documents suggest or teach towards the production of a genetically modified mammal expressing an apoL-I polynucleotide/polypeptide. In this regard, documents D6 and D7 each disclose genetically modified mammals expressing different apolipoproteins (A, B or E) for investigating neuronal/atherosclerotic diseases. There is no suggestion in these documents, however, of expression of apoL-I. Moreover, in the absence of any further disclosure in the prior art relating to apoL-I as a trypanolytic factor, it must be concluded that there was no motivation for the skilled man to produce genetically modified mammals expressing an apoL-I polynucleotide/polypeptide. The present Applicant's disclosure that such mammals can be used as models for studying Trypanosomal diseases does not appear to have been predictable on the basis of the prior art. Thus the subject matter of Claims 14 to 16 appears to be inventive.

EXHIBIT B

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
12 February 2004 (12.02.2004)

PCT

(10) International Publication Number
WO 2004/012757 A3

(51) International Patent Classification⁷: A61K 38/17, A61P 33/02, A01K 67/027, G01N 33/92

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(72) Inventors; and

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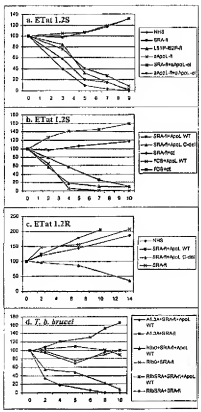
(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),

[Continued on next page]

(54) Title: APOLIPOPROTEIN L-I FOR THE TREATMENT OR DIAGNOSIS OF PRYPANOSOMALDISEASES

(57) Abstract: The present invention is related to a composition comprising apolipoprotein L-I, the use of apolipoprotein L-I or a derivated polypeptide for the diagnostic, the treatment and/or the prevention of diseases induced in mammals by Trypanosoma. Another aspect is related to a transgenic non-human mammal comprising a polynucleotide expressing said apolipoprotein or a derivated polypeptide and which is tolerant or resistant to said Trypanosoma infection.



WO 2004/012757 A3

European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
15 April 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/BE 03/00131

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K38/17 A61P33/02 A01K67/027 G01N33/92

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TYTLER E M ET AL: "Reconstitution of the trypanolytic factor from components of a subspecies of human high-density lipoproteins." MOLECULAR AND BIOCHEMICAL PARASITOLOGY. NETHERLANDS JAN 1995, vol. 69, no. 1, January 1995 (1995-01), pages 9-17, XP001155959 ISSN: 0166-6851 abstract Introduction and Discussion particularly the final paragraph	1-10

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 February 2004	10. 03. 2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Pilling, S

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	MILNER J D ET AL: "Expression and localization of serum resistance associated protein in Trypanosoma brucei rhodesiense." MOLECULAR AND BIOCHEMICAL PARASITOLOGY. NETHERLANDS 30 NOV 1999, vol. 104, no. 2, 30 November 1999 (1999-11-30), pages 271-283, XP001155961 ISSN: 0166-6851 abstract introduction particularly the first paragraph and the Discussion particularly the last paragraph	1-10
A	DUCHATEAU P N ET AL: "Apolipoprotein L gene family: Tissue-specific expression, splicing, promoter regions;discovery of a new gene" JOURNAL OF LIPID RESEARCH, BETHESDA, MD, US, vol. 42, no. 4, April 2001 (2001-04), pages 620-630, XP002247906 ISSN: 0022-2275 the whole document	1-10
A	PAGE N M ET AL: "The human apolipoprotein L gene cluster: identification, classification, and sites of distribution." GENOMICS. UNITED STATES 15 MAY 2001, vol. 74, no. 1, 15 May 2001 (2001-05-15), pages 71-78, XP001155958 ISSN: 0888-7543 the whole document	1-10
P,X	VANHAMME LUC ET AL: "Apolipoprotein L-I is the trypanosome lytic factor of human serum." NATURE. ENGLAND 6 MAR 2003, vol. 422, no. 6927, 6 March 2003 (2003-03-06), pages 83-87, XP001155956 ISSN: 0028-0836 abstract	1-10
A	US 5 767 337 A (ROSES ALLEN D ET AL) 16 June 1998 (1998-06-16) the whole document	14-16
A	WO 99/35241 A (EMMANUEL FLORENCE ; HOUDEBINE LOUIS MARIE (FR); ROUY DIDIER (FR); DENE) 15 July 1999 (1999-07-15) the whole document	14-16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/BE 03/00131

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

1-10,14-16

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-10

   pharmaceutical compositions/uses comprising apolipoprotein L-I (apoL-I), an active fragment thereof, a polynucleotide encoding apoL-I, a cell transformed with the latter polynucleotide or an apoL-I inhibitor

2. claims: 11-13

   diagnostic kits comprising apoL-I, a fragment thereof, a polynucleotide encoding apoL-I or an apoL-I inhibitor

3. claims: 14-16

   non-human genetically modified mammals which express a polynucleotide encoding apoL-I or a fragment thereof and are resistant to Trypanosoma diseases

4. claims: 17,18

   solid supports/methods for recovering apoL-I from a mammal using an immobilised apoL-I inhibitor